GC527

Mutant Proteins Having Lower Allergenic Response in Humans & Methods for Constructing, Identifying & Producing Such Proteins
Estell et al.
SN# 09/062,872

APPROVED BY DRAFTSMAN | O.G. FIG. CLASS | SUBCLASS

5 ↓ P … 3 ↓ … 4 ↓ … RBS … -107 Met

1 GGTCTACTAAAATATTATTCCATACTATACAATTAATACACAGAATAATCTGTCTATTGGTTATTCTGCAAATGAAAAAAAGGAGAGGATAAAGA GTG

							-100	PRE								-90									
	Arg	Gly	Lys	Lys	Val	Trp	Ile	Ser	Leu	Leu	Phe	Ala	Leu	Ala	Leu	Ile	Phe	Thr	Met	Ala	Phe	Gly	Ser	Thr	Ser
99	AGA	GGC	AAA	AAA	GTA	TGG	ATC	AGT	TTG	CTG	TTT	GCT	TTA	GCG	TTA	ATC	TTT	ACG	ATG	GCG	TTC	GGC	AGC	ACA	TCC
		-80										-70		PRO								-60			
	Ser	Ala	Gln	Ala	Ala	Gly	Lys	Ser	Asn	Gly	Glu	Lys	Lys	Tyr	Ile	Val	Gly	Phe	Lys	Gln	Thr	Met	Ser	Thr	Met
174	TCT	GCC	CAG	GCG	GCA	GGG	AAA	TCA	AAC	GGG	GAA	AAG	AAA	TAT	ATT	GTC	GGG	TTT	AAA	CAG	ACA	ATG	AGC	ACG	ATG
							-50										-40								
	Ser	Ala	Ala	Lys	Lys	Lys	Asp	Val	Ile	Ser	Glu	Lys	Gly	Gly	Lys	Val	Gln	Lys	Gln	Phe	Lys	Tyr	Val	Asp	Ala
249	AGC	GCC	GCT	AAG	AAG	AAA	GAT	GTC	ATT	TCT	GAA	AAA	GGC	GGG	AAA	GTG	CAA	AAG	CAA	TTC	AAA	TAT	GTA	GAC	GCA
		-30										-20										-10			
	Ala	Ser	Ala	Thr	Leu	Asn	Glu	Lys	Ala	Val	Lys	Glu	Leu	Lys	Lys	Asp	Pro	Ser	Val	Ala	Tyr	Val	Glu	Glu	Asp
324	GCT	TCA	GCT	ACA	TTA	AAC	GAA	AAA	GCT	GTA	AAA	GAA	TTG	AAA	AAA	GAC	CCG	AGC	GTC	GCT	TAC	GTT	GAA	GAA	GAT
						-1	→ 1 MAT									10									
	His	Val	Ala	His	Ala	Tyr	Ala	Gln	Ser	Val	Pro	Tyr	Gly	Val	Ser	Gln	Ile	Lys	Ala	Pro	Ala	Leu	His	Ser	Gln
399	CAC	GTA	GCA	CAT	GCG	TAC	GCG	CAG	TCC	GTG	CCT	TAC	GGC	GTA	TCA	CAA	ATT	AAA	GCC	CCT	GCT	CTG	CAC	TCT	CAA
	20										30										40				
	Gly	Tyr	Thr	Gly	Ser	Asn	Val	Lys	Val	Ala	Val	Ile	Asp	Ser	Gly	Ile	Asp	Ser	Ser	His	Pro	Asp	Leu	Lys	Val
474	GGC	TAC	ACT	GGA	TCA	AAT	GTT	AAA	GTA	GCG	GTT	ATC	GAC	AGC	GGT	ATC	GAT	TCT	TCT	CAT	CCT	GAT	TTA	AAG	GTA

FIG._1B - 1

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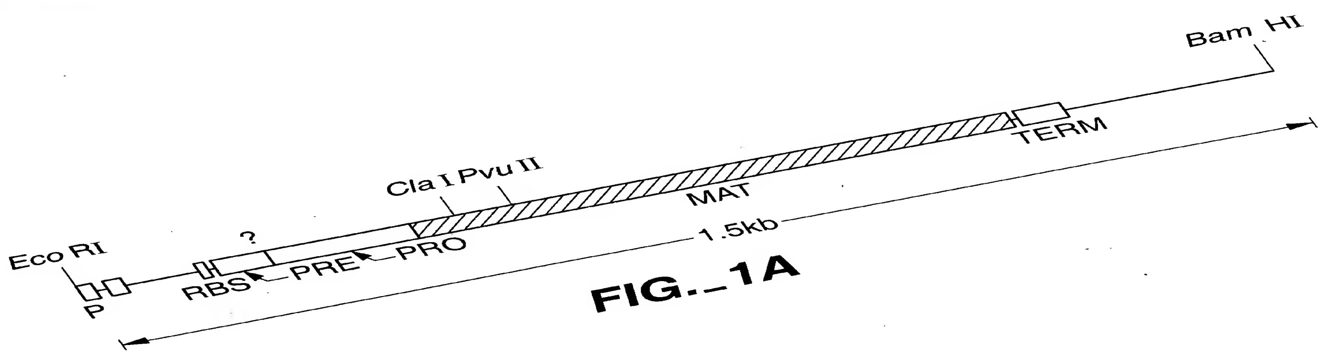

FIG._1A

Mutant Proteins Having Lower Allergenic
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50 (Met) 60 (Asp)
Pro (over Asn) Asn (over Pro) Asp (over Asn)
549 Ala Gly Gly Ala Ser Met Val Pro Ser Glu Thr Asn Pro Phe Gln Asp Asn Asn Ser His Gly Thr His Val Ala
GCA GGC GGA GCC AGC ATG GTT CCT TCT GAA ACA AAT CCT TTC CAA GAC AAC AAC TCT CAC GGA ACT CAC GTT GCC

70 (Gly) 80 (Gly) 90 (Leu)
Ser (over Ala) Ala (over Ser)
624 Gly Thr Val Ala Ala Leu Asn Asn Ser Ile Gly Val Leu Gly Val Ala Pro Ser Ala Ser Leu Tyr Ala Val Lys
GGC ACA GTT GCG GCT CTT AAT AAC TCA ATC GGT GTA TTA GGC GTT GCG CCA AGC GCA TCA CTT TAC GCT GTA AAA

100 (Gly) 110 (Gly)
Asp (over Ala) Ala (over Asp)
699 Val Leu Gly Ala Asp Gly Ser Gly Gln Tyr Ser Trp Ile Ile Asn Gly Ile Glu Trp Ala Ile Ala Asn Asn Met
GTT CTC GGT GCT GAC GGT TCC GGC CAA TAC AGC TGG ATC ATT AAC GGA ATC GAG TGG GCG ATC GCA AAC AAT ATG

120 (Asp) 130 (Ser) 140 (Asp)
774 Asp Val Ile Asn Met Ser Leu Gly Gly Pro Ser Gly Ser Ala Ala Leu Lys Ala Ala Val Asp Lys Ala Val Ala
GAC GTT ATT AAC ATG AGC CTC GGC GGA CCT TCT GGT TCT GCT GCT TTA AAA GCG GCA GTT GAT AAA GCC GTT GCA

150 (Val) 160 (Gly)
Ser (over Thr) Thr (over Ser)
849 Ser Gly Val Val Val Val Ala Ala Ala Gly Asn Glu Gly Thr Ser Gly Ser Ser Ser Thr Val Gly Tyr Pro Gly
TCC GGC GTC GTA GTC GTT GCG GCA GCC GGT AAC GAA GGC ACT TCC GGC AGC TCA AGC ACA GTG GGC TAC CCT GGT

170 (Lys) 180 (Val) 190 (Ser)
924 Lys Tyr Pro Ser Val Ile Ala Val Gly Ala Val Asp Ser Ser Asn Gln Arg Ala Ser Phe Ser Ser Val Gly Pro
AAA TAC CCT TCT GTC ATT GCA GTA GGC GCT GTT GAC AGC AGC AAC CAA AGA GCA TCT TTC TCA AGC GTA GGA CCT

200 (Ala) 210 (Pro)
999 Glu Leu Asp Val Met Ala Pro Gly Val Ser Ile Gln Ser Thr Leu Pro Gly Asn Lys Tyr Gly Ala Tyr Asn Gly
GAG CTT GAT GTC ATG GCA CCT GGC GTA TCT ATC CAA AGC ACG CTT CCT GGA AAC AAA TAC GGG GCG TAC AAC GGT

220 (Thr) 230 (Ala) 240 (Asn)
1074 Thr Ser Met Ala Ser Pro His Val Ala Gly Ala Ala Ala Leu Ile Leu Ser Lys His Pro Asn Trp Thr Asn Thr
ACG TCA ATG GCA TCT CCG CAC GTT GCC GGA GCG GCT GCT TTG ATT CTT TCT AAG CAC CCG AAC TGG ACA AAC ACT

FIG._1B - 2

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```
                                  250                                                      260
          Gln  Val  Arg  Ser  Ser  Leu  Gln  Asn  Thr  Thr  Thr  Lys  Leu  Gly  Asp  Ser  Phe  Tyr  Tyr  Gly  Lys  Gly  Leu  Ile  Asn
                                       Glu
1149      CAA  GTC  CGC  AGC  AGT  TTA  GAA  AAC  ACC  ACT  ACA  AAA  CTT  GGT  GAT  TCT  TTC  TAC  TAT  GGA  AAA  GGG  CTG  ATC  AAC

          270                      275                  TERM
          Val  Gln  Ala  Ala  Ala  Gln  OC
1224      GTA  CAG  GCG  GCA  GCT  CAG  TAA  AACATAAAAAACCGGCCTTGGCCCCGCCGGTTTTTTATTTTTCTTCCTCCGCATGTTCAATCCGCTCC

1316      ATAATCGACGGATGGCTCCCTCTGAAAATTTTAACGAGAAACGGCGGGTTGACCCGGCTCAGTCCCGTAACGGCCAAGTCCTGAAACGTCTCAATCGCCG

1416      CTTCCCGGTTTCCGGTCAGCTCAATGCCGTAACGGTCGGCGGCGTTTTCCTGATACCGGGAGACGGCATTCGTAATCGGATC
```

FIG._1B - 3

FIG._1B - 1
FIG._1B - 2
FIG._1B - 3

FIG._1B

CONSERVED RESIDUES IN SUBTILISINS FROM *BACILLUS AMYLOLIQUEFACIENS*

1								10												20
A	Q	S	V	P	.	G	.	.	.	.	.	A	P	A	.	H	.	.	G	
21								30												40
.	T	G	S	.	V	K	V	A	V	.	D	.	G	.	.	.	.	H	P	
41								50												60
D	L	.	.	.	G	G	A	S	.	V	P	.	.	.	.	.	.	Q	D	
61								70												80
.	N	.	H	G	T	H	V	A	G	T	.	A	A	L	N	N	S	I	G	
81								90												100
V	L	G	V	A	P	S	A	.	L	Y	A	V	K	V	L	G	A	.	G	
101								110												120
S	G	.	.	S	.	L	.	.	G	.	E	W	A	.	N	.	.	.	.	
121								130												140
V	.	N	.	S	L	G	.	P	S	.	S	.	.	.	.	.	A	.	.	
141								150												160
.	.	.	.	.	.	G	V	.	V	V	A	A	.	G	N	.	G	.	.	
161								170												180
.	.	.	.	.	.	.	Y	P	.	.	Y	.	.	.	.	A	V	G	A	.
181								190												200
D	.	.	N	.	.	A	S	F	S	.	.	G	.	.	L	D	.	.	A	
201								210												220
P	G	V	.	.	Q	S	T	.	P	G	.	.	Y	.	.	.	N	G	T	
221								230												240
S	M	A	.	P	H	V	A	G	A	A	A	L	.	.	.	K	.	.	.	
241								250												260
W	.	.	.	Q	.	R	.	.	L	.	N	T	.	.	.	L	G	.	.	
261								270												
.	.	Y	G	.	G	L	.	N	.	.	A	A	.	.						

FIG._2

COMPARISION OF SUBTILISIN SEQUENCES FROM:
B.amyloliquefaciens
B.subtilis
B.licheniformis
B.lentus

FIG._3A

```
01                  10                  20                  30
A Q S V P Y G V S Q I K A P A L H S Q G Y T G S N V K V A V I D S G I D S S H P
A Q S V P Y G I S Q I K A P A L H S Q G Y T G S N V K V A V I D S G I D S S H P
A Q T V P Y G I P L I K A D K V Q A Q G F K G A N V K V A V L D T G I Q A S H P
A Q S V P W G I S R V Q A P A A H N R G L T G S G V K V A V L D T G I S T * H P

41                  50                  60                  70
D L K V A G G A S M V P S E T N P F Q D N N S H G T H V A G T V A A L N N S I G
D L N V R G G A S F V P S E T N P Y Q D G S S H G T H V A G T I A A L N N S I G
D L N V V G G A S F V A G E A Y N * T D G N G H G T H V A G T V A A L D N T T G
D L N I R G G A S F V P G E * P S T Q D G N G H G T H V A G T I A A L N N S I G

81                  90                  100                 110
V L G V A P S A S L Y A V K V L G A D G S G Q Y S W I I N G I E W A I A N N M D
V L G V S P S A S L Y A V K V L D S T G S G Q Y S W I I N G I E W A I S N N M D
V L G V A P S V S L Y A V K V L N S S G S G S Y S G I V S G I E W A T T N G M D
V L G V A P S A E L Y A V K V L G A S G S G S V S S I A Q G L E W A G N N G M H

121                 130                 140                 150
V I N M S L G G P S G S A A L K A A V D K A V A S G V V V V A A A G N E G T S G
V I N M S L G G P T G S T A L K T V V D K A V S S G I V V A A A A G N E G S S G
V I N M S L G G A S G S T A M K Q A V D N A Y A R G V V V V A A A G N S G N S G
V A N L S L G S P S P S A T L E Q A V N S A T S R G V L V V A A S G N S G A G S
```

```
161                 170                 180                 190
S S S T V G Y P G K Y P S V I A V G A V D S S N Q R A S F S S V G P E L D V M A
S T S T V G Y P A K Y P S T I A V G A V N S S N Q R A S F S S A G S E L D V M A
S T N T I G Y P A K Y D S V I A V G A V D S N S N R A S F S S V G A E L E V M A
* * * * I S Y P A R Y A N A M A V G A T D Q N N N R A S F S Q Y G A G L D I V A

201                 210                 220                 230
P G V S I Q S T L P G N K Y G A Y N G T S M A S P H V A G A A A L I L S K H P N
P G V S I Q S T L P G G T Y G A Y N G T S M A T P H V A G A A A L I L S K H P T
P G A G V Y S T Y P T N T Y A T L N G T S M A S P H V A G A A A L I L S K H P N
P G V N V Q S T Y P G S T Y A S L N G T S M A T P H V A G A A A L V K Q K N P S

241                 250                 260                 270
W T N T Q V R S S L E N T T T K L G D S F Y Y G K G L I N V Q A A A Q
W T N A Q V R D R L E S T A T Y L G N S F Y Y G K G L I N V Q A A A Q
L S A S Q V R N R L S S T A T Y L G S S F Y Y G K G L I N V E A A A Q
W S N V Q I R N H L K N T A T S L G S T N L Y G S G L V N A E A A T R
```

FIG._3B

FIG._3

FIG._3A

FIG._3B

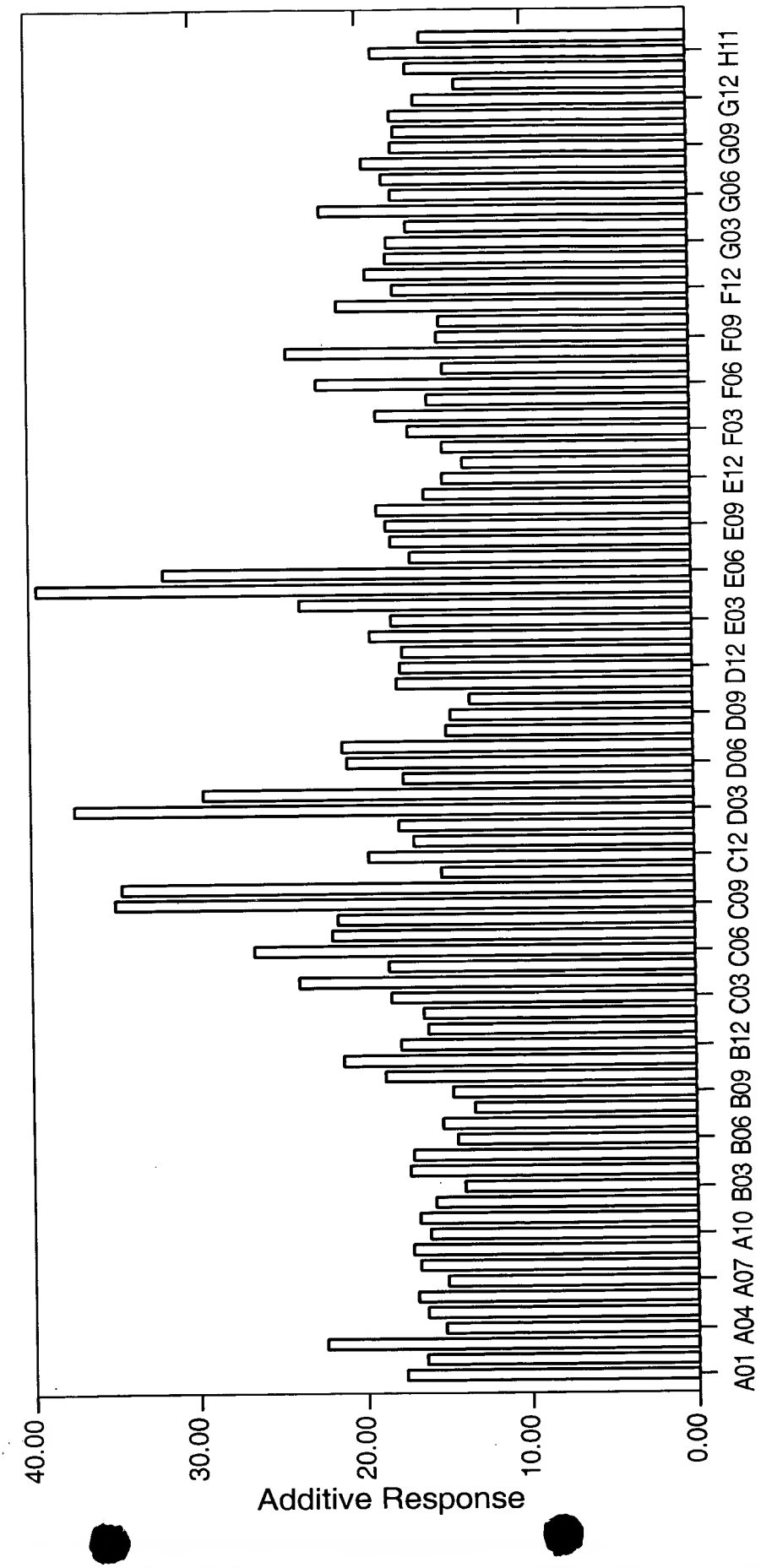

FIG._4

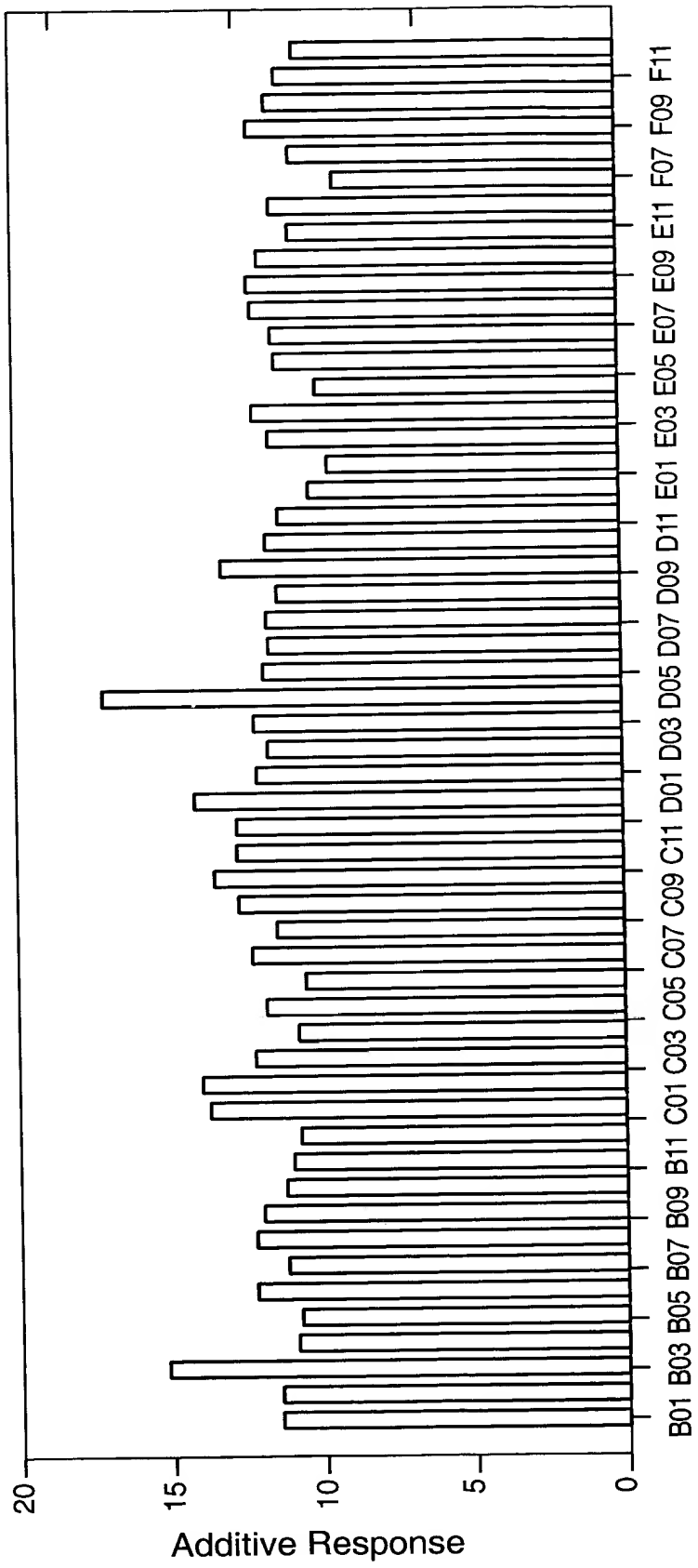

FIG._5

1	A12	IKDFHVYFRESRDAG	49	E12	SATSRGVLVVAASGN
2	A11	LEQAVNSATSRGVLV	50	E11	SRGVLVVAASGNSGA
3	A10	AQSVPWGISRVQAPA	51	E10	VLVVAASGNSGAGSI
4	A9	VPWGISRVQAPAAHN	52	E9	VAASGNSGAGSISYP
5	A8	GISRVQAPAAHNRGL	53	E8	SGNSGAGSISYPARY
6	A7	RVQAPAAHNRGLTGS	54	E7	SGAGSISYPARYANA
7	A6	APAAHNRGLTGSGVK	55	E6	GSISYPARYANAMAV
8	A5	AHNRGLTGSGVKVAV	56	E5	SYPARYANAMAVGAT
9	A4	RGLTGSGVKVAVLDT	57	E4	ARYANAMAVGATDQN
10	A3	TGSGVKVAVLDTGIS	58	E3	ANAMAVGATDQNNNR
11	A2	GVKVAVLDTGISTHP	59	E2	MAVGATDQNNNRASF
12	A1	VAVLDTGISTHPDLN	60	E1	GATDQNNNRASFSQY
13	B12	LDTGISTHPDLNIRG	61	F12	DQNNNRASFSQYGAG
14	B11	GISTHPDLNIRGGAS	62	F11	NNRASFSQYGAGLDI
15	B10	THPDLNIRGGASFVP	63	F10	ASFSQYGAGLDIVAP
16	B9	DLNIRGGASFVPGEP	64	F9	SQYGAGLDIVAPGVN
17	B8	IRGGASFVPGEPSTQ	65	F8	GAGLDIVAPGVNVQS
18	B7	GASFVPGEPSTQDGN	66	F7	LDIVAPGVNVQSTYP
19	B6	FVPGEPSTQDGNGHG	67	F6	VAPGVNVQSTYPGST
20	B5	GEPSTQDGNGHGTHV	68	F5	GVNVQSTYPGSTYAS
21	B4	STQDGNGHGTHVAGT	69	F4	VQSTYPGSTYASLNG
22	B3	DGNGHGTHVAGTIAA	70	F3	TYPGSTYASLNGTSM
23	B2	GHGTHVAGTIAALNN	71	F2	GSTYASLNGTSMATP
24	B1	THVAGTIAALNNSIG	72	F1	YASLNGTSMATPHVA
25	C12	AGTIAALNNSIGVLG	73	G12	LNGTSMATPHVAGAA
26	C11	IAALNNSIGVLGVAP	74	G11	TSMATPHVAGAAALV
27	C10	LNNSIGVLGVAPSAE	75	G10	ATPHVAGAAALVKQK
28	C9	SIGVLGVAPSAELYA	76	G9	HVAGAAALVKQKNPS
29	C8	VLGVAPSAELYAVKV	77	G8	GAAALVKQKNPSWSN
30	C7	VAPSAELYAVKVLGA	78	G7	ALVKQKNPSWSNVQI
31	C6	SAELYAVKVLGASGS	79	G6	KQKNPSWSNVQIRNH
32	C5	LYAVKVLGASGSGSV	80	G5	NPSWSNVQIRNHLKN
33	C4	VKVLGASGSGSVSSI	81	G4	WSNVQIRNHLKNTAT
34	C3	LGASGSGSVSSIAQG	82	G3	VQIRNHLKNTATSLG
35	C2	SGSGSVSSIAQGLEW	83	G2	RNHLKNTATSLGSTN
36	C1	GSVSSIAQGLEWAGN	84	G1	LKNTATSLGSTNLYG
37	D12	SSIAQGLEWAGNNGM	85	H12	TATSLGSTNLYGSGL
38	D11	AQGLEWAGNNGMHVA	86	H11	SLGSTNLYGSGLVNA
39	D10	LEWAGNNGMHVANLS	87	H10	STNLYGSGLVNAEAA
40	D9	AGNNGMHVANLSLGS	88	H9	NLYGSGLVNAEAATR
41	D8	NGMHVANLSLGSPSP			
42	D7	HVANLSLGSPSPSAT			
43	D6	NLSLGSPSPSATLEQ			
44	D5	LGSPSPSATLEQAVN			
45	D4	PSPSATLEQAVNSAT			
46	D3	SATLEQAVNSATSRG			
47	D2	LEQAVNSATSRGVLV			
48	D1	AVNSATSRGVLVVAA			

FIG._6A

1	A12	IKDFHVYFRESRDAG	49	E12	KKIDVLNLSIGGPDF
2	A11	DAELHIFRVFTNNQV	50	E11	DVLNLSIGGPDFMDH
3	A10	PLRRASLSLGSGFWH	51	E10	NLSIGGPDFMDHPFV
4	A9	RASLSLGSGFWHATG	52	E9	IGGPDFMDHPFVDKV
5	A8	LSLGSGFWHATGRHS	53	E8	PDFMDHPFVDKVWEL
6	A7	GSGFWHATGRHSSRR	54	E7	MDHPFVDKVWELTAN
7	A6	FWHATGRHSSRRLLR	55	E6	PFVDKVWELTANNVI
8	A5	ATGRHSSRRLLRAIP	56	E5	DKVWELTANNVIMVS
9	A4	RHSSRRLLRAIPRQV	57	E4	WELTANNVIMVSAIG
10	A3	SRRLLRAIPRQVAQT	58	E3	TANNVIMVSAIGNDG
11	A2	LLRAIPRQVAQTLQA	59	E2	NVIMVSAIGNDGPLY
12	A1	AIPRQVAQTLQADVL	60	E1	MVSAIGNDGPLYGTJ
13	B12	RQVAQTLQADVLWQM	61	F12	AIGNDGPLYGTLNNP
14	B11	AQTLQADVLWQMGYT	62	F11	NDGPLYGTLNNPADQ
15	B10	LQADVLWQMGYTGAN	63	F10	PLYGTLNNPADQMDV
16	B9	DVLWQMGYTGANVRV	64	F9	GTLNNPADQMDVIGV
17	B8	WQMGYTGANVRVAVF	65	F8	NNPADQMDVIGVGGI
18	B7	GYTGANVRVAVFDTG	66	F7	ADQMDVIGVGGIDFE
19	B6	GANVRVAVFDTGLSE	67	F6	MDVIGVGGIDFEDNI
20	B5	VRVAVFDTGLSEKHP	68	F5	IGVGGIDFEDNIARF
21	B4	AVFDTGLSEKHPHFK	69	F4	GGIDFEDNIARFSSR
22	B3	DTGLSEKHPHFKNVK	70	F3	DFEDNIARFSSRGMT
23	B2	LSEKHPHFKNVKERT	71	F2	DNIARFSSRGMTTWE
24	B1	KHPHFKNVKERTNWT	72	F1	ARFSSRGMTTWELPG
25	C12	HFKNVKERTNWTNER	73	G12	SSRGMTTWELPGGYG
26	C11	NVKERTNWTNERTLD	74	G11	GMTTWELPGGYGRMK
27	C10	ERTNWTNERTLDDGL	75	G10	TWELPGGYGRMKPDI
28	C9	NWTNERTLDDGLGHG	76	G9	LPGGYGRMKPDIVTY
29	C8	NERTLDDGLGHGTFV	77	G8	GYGRMKPDIVTYGAG
30	C7	TLDDGLGHGTFVAGV	78	G7	RMKPDIVTYGAGVRG
31	C6	DGLGHGTFVAGVIAS	79	G6	PDIVTYGAGVRGSGV
32	C5	GHGTFVAGVIASMRE	80	G5	VTYGAGVRGSGVKGG
33	C4	TFVAGVIASMRECQG	81	G4	GAGVRGSGVKGGCRA
34	C3	AGVIASMRECQGFAP	82	G3	VRGSGVKGGCRALSG
35	C2	IASMRECQGFAPDAE	83	G2	SGVKGGCRALSGTSV
36	C1	MRECQGFAPDAELHI	84	G1	KGGCRALSGTSVASP
37	D12	CQGFAPDAELHIFRV	85	H12	CRALSGTSVASPVVA
38	D11	FAPDAELHIFRVFTN	86	H11	LSGTSVASPVVAGAV
39	D10	DAELHIFRVFTNNQV	87	H10	TSVASPVVAGAVTLL
40	D9	LHIFRVFTNNQVSYT	88	H9	ASPVVAGAVTLLVST
41	D8	FRVFTNNQVSYTSWF	89	H8	VVAGAVTLLVSTVQK
42	D7	FTNNQVSYTSWFLDA	90	H7	GAVTLLVSTVQKREL
43	D6	NQVSYTSWFLDAFNY	91	H6	TLLVSTVQKRELVNP
44	D5	SYTSWFLDAFNYAIL	92	H5	VSTVQKRELVNPASM
45	D4	SWFLDAFNYAILKKI	93	H4	VQKRELVNPASMKQA
46	D3	LDAFNYAILKKIDVL	94	H3	RELVNPASMKQALIA
47	D2	FNYAILKKIDVLNLS	95	H2	VNPASMKQALIASAR
48	D1	AILKKIDVLNLSIGG	96	H1	ASMKQALIASARRLP

FIG._6B

97	I12	IKDFHVYFRESRDAG
98	I11	DAELHIFRVFTNNQV
99	I10	KQALIASARRLPGVN
100	I9	LIASARRLPGVNMFE
101	I8	SARRLPGVNMFEQGH
102	I7	RLPGVNMFEQGHGKL
103	I6	GVNMFEQGHGKLDLL
104	I5	MFEQGHGKLDLLRAY
105	I4	QGHGKLDLLRAYQIL
106	I3	GKLDLLRAYQILNSY
107	I2	DLLRAYQILNSYKPQ
108	I1	RAYQILNSYKPQASL
109	J12	QILNSYKPQASLSPS
110	J11	NSYKPQASLSPSYID
111	J10	KPQASLSPSYIDLTE
112	J9	ASLSPSYIDLTECPY
113	J8	SPSYIDLTECPYMWP
114	J7	YIDLTECPYMWPYCS
115	J6	LTECPYMWPYCSQPI
116	J5	CPYMWPYCSQPIYYG

FIG._6C

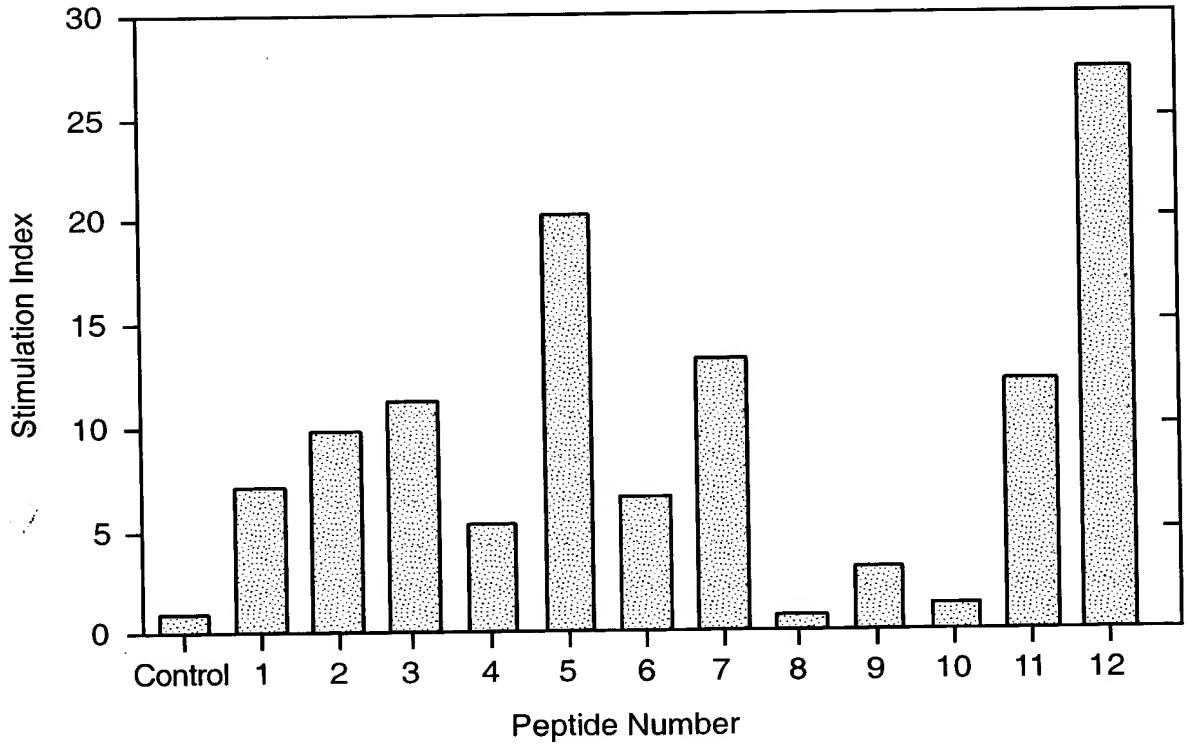

FIG._10

MKLVNIWLLLLVVLLCGKKHLGDRLEKKSFEKAPCPGCSHLTLKVEFSSTVVEYEYIVAFNGYFT
AKARNSFISSALKSSEVDNWRIIPRNNPSSDYPSDFEVIQIKEKQKAGLLTLEDHPNIKRVTPQR
KVFRSLKYAESDPTVPCNETRWSQKWQSSRPLRRASLSLGSGFWHATGRHSSRRLLRAIPRQVAQ
TLQADVLWQMGYTGANVRVAVFDTGLSEKHPHFKNVKERTNWTNERTLDDGLGHGTFVAGVIASM
RECQGFAPDAELHIFRVFTNNQVSYTSWFLDAFNYAILKKIDVLNLSIGGPDFMDHPFVDKVWEL
TANNVIMVSAIGNDGPLYGTLNNPADQMDVIGVGGIDFEDNIARFSSRGMTTWELPGGYGRMKPD
IVTYGAGVRGSGVKGGCRALSGTSVASPVVAGAVTLLVSTVQKRELVNPASMKQALIASARRLPG
VNMFEQGHGKLDLLRAYQILNSYKPQASLSPSYIDLTECPYMWPYCSQPIYYGGMPTVVNVTILN
GMGVTGRIVDKPDWQPYLPQNGDNIEVAFSYSSVLWPWSGYLAISISVTKKAASWEGIAQGHVMI
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ANHDMYYASGCSIAKFPEDGVVITQTFKDQGLEVLKQETAVVENVPILGLYQIPAEGGGRIVLYG
DSNCLDDSHRQKDCFWLLDALLQYTSYGVTPPSLSHSGNRQRPPSGAGSVTPERMEGNHLHRYSK
VLEAHLGDPKPRPLPACPRLSWAKPQPLNETAPSNLWKHQKLLSIDLDKVVLPNFRSNRPQVRPL
SPGESGAWDIPGGIMPGRYNQEVGQTIPVFAFLGAMVVLAFFVVQINKAKSRPKRRKPRVKRPQL
MQQVHPPKTPSV

FIG._7

FIG._8

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                  10        20        30        40        50
BPN'      AQSVPYGVSQ-IKAPALHSQGYTGSNVKVAVIDSGIDSSHPDLK-VAGGA  48
SAVINASE  AQSVPWGISR-VQAPAAHNRGLTGSGVKVAVLDTGI-STHPDLN-IRGGA  47
S2HSBT    -RAIPRQVAQTLQADVLWQMGYTGANVRVAVFDTGLSEKHPHFKNVKERT  49

                  60        70        80        90       100
BPN'      SMVPSETNPFQDNNSHGTHVAGTVAALNNSIGVLGVAPSASLYAVKVLGA  98
SAVINASE  SFVPGEPST-QDGNGHGTHVAGTIAALNNSIGVLGVAPSAELYAVKVLGA  96
S2HSBT    NW--TNERTLDDGLGHGTFVAGVIASMRECQGF---APDAELHIFRVFTN  94

                 110       120       130       140       150
BPN'      DGSGQYSWIINGIEWAIANNMDVINMSLGGPS-GSAALKAAVDKAVASGV 147
SAVINASE  SGSGSVSSIAQGLEWAGNNGMHVANLSLGSPS-PSATLEQAVNSATSRGV 145
S2HSBT    NQVSYTSWFLDAFNYAILKKIDVLNLSIGGPDFMDHPFVDKVWELTANNV 144

                 160       170       180       190       200
BPN'      VVVAAAGNEGTSGSSSTVGYPGKYPSVIAVGAVDSSNQRASFSSVGPEL- 197
SAVINASE  LVVAASGNSGA----GSISYPARYANAMAVGATDQNNNRASFSQYGAGL- 191
S2HSBT    IMVSAIGNDGP--LYGTLNNPADQMDVIGVGGIDFEDNIARFSSRGMTTW 192

                 210       220       230       240       250
BPN'      ------------DVMAPGVSIQSTLPGNKYGAYNGTSMASPHVAGAAALIL 235
SAVINASE  ------------DIVAPGVNVQSTYPGSTYASLNGTSMATPHVAGAAALVK 229
S2HSBT    ELPGGYGRMKPDIVTYGAGVRGSGVKGGCRALSGTSVASPVVAGAVTLLV 242

                 260       270       280       290
BPN'      SKHPNWTNTQ---VRSSLENTTTKLGDSFYYGKGLINVQAAAQ         275
SAVINASE  QKNPSWSNVQ---IRNHLKNTATSLGSTNLYGSGLVNAEAATR        269
S2HSBT    STVQKRELVNPASMKQALIASARRLPGVNMFEQG-----HGKL         280
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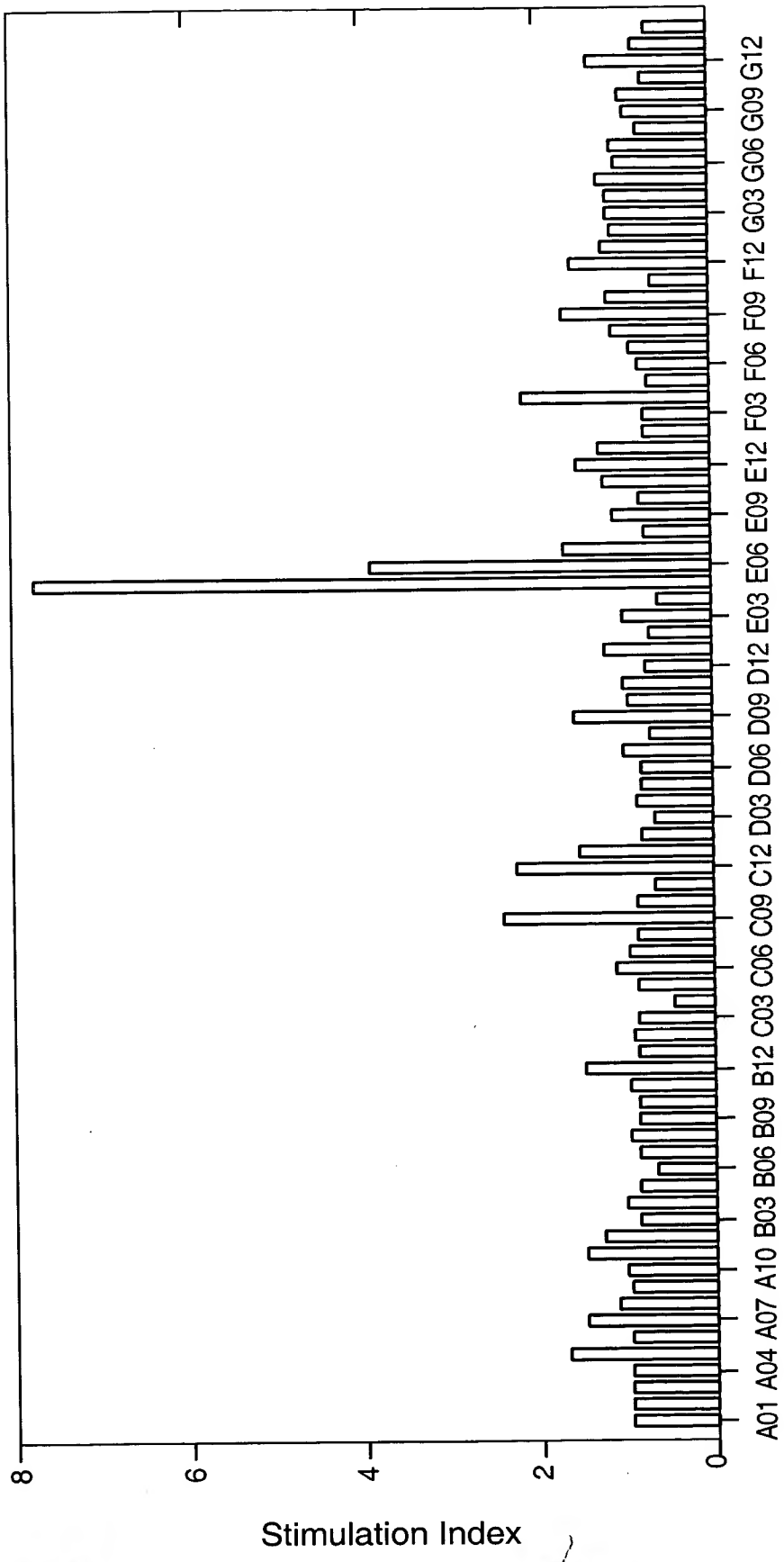

FIG._9

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